REMARKS

The Official action mailed November 10, 2004, has been reviewed and carefully considered. Claims 3, 10, 13, 15, 21, 43-45, 90, 93-97, 101 and 102 have now been canceled. New claims 114-123 have been added. The amendments to independent claims 1, 16, 53 and 88 find support throughout the specification. For example, claims 1, 16, 53 and 88 have been amended to incorporate the subject matter previously recited in claim 43, now canceled. Support for the amendment to claims 24 and 32 is found in the specification on page 9, lines 16-17. Support for new claims 114, 115 and 119 is found in the specification, for example, at page 4, lines 29-32. Support for new claim 116 is found in the specification, for example, at page 14, lines 31-36. Support for new claims 117 and 118 is found in the specification, for example, in Example 7 beginning on page 29. Support for new claims 120 and 121 is found throughout the specification. Support for new claim 122 is found in the specification, for example, at page 17, lines 29-33. Support for new claim 123 is found in the specification, for example, at page 4, lines 20-21. Entry of these amendments and new claims is respectfully requested.

35 U.S.C. §102 rejections

Lampkin et al.

Claims 1, 2, 4, 6, 7, 13, 15 and 88 have been rejected under 35 U.S.C. §102(b) over Lampkin et al. Applicants continue to maintain that Lampkin et al. fails to disclose comparing and correlating results from corresponding assigned locations of different substantial copies as recited in independent claims 1 and 88. However, in order to advance prosecution, independent claims 1 and 88 have been amended to include a further step specifying additional analysis that is performed based on the correlations or results obtained from the array. Lampkin et al. does not disclose or suggest that any of the specifically claimed additional analyses could be performed using the sample blocks obtained according to Lampkin et al.

Claims 1 and 88 have also been amended to include subjecting a first substantial copy of the recipient array to a first assay and subjecting at least one successive second substantial copy of the recipient array to at least one second assay, wherein the first assay is different than the second assay. Claims 1 and 88 no longer recite "performing a biological analysis of each

substantial copy." Accordingly, the visual inspection analysis that the examiner asserts on page 4 of the Office action is disclosed by Lampkin et al. is not relevant to claims 1 and 88.

In addition, new dependent claim 120 indicates that at least the first assay or the second assay comprises a nucleic acid analysis, and new dependent claim 121 indicates that at least one of the first agent or the second agent comprises a nucleic acid probe. Lampkin et al. only mentions staining with histochemical or immunocytochemical reagents (page 122, first column). There is no mention in Lampkin et al. of any type of nucleic acid analysis. Hence, Lampkin et al. does not anticipate or render obvious claims 120 and 121.

Kraaz et al.

Claims 1-7, 9-15, 49 and 88 have been rejected under 35 U.S.C. §102(b) over Kraaz et al. Applicants continue to maintain that Kraaz et al. fails to disclose comparing and correlating results from corresponding assigned locations of different substantial copies as recited in independent claims 1 and 88. However, in order to advance prosecution, claims 1 and 88 have been amended to include a further step specifying additional analysis that is performed based on the correlations or results obtained from the array. Kraaz et al. does not disclose or suggest that any of the specifically claimed additional analyses could be performed using the sample blocks obtained according to Kraaz et al.

Claims 1 and 88 have also been amended to include subjecting a first substantial copy of the recipient array to a first assay and subjecting at least one successive second substantial copy of the recipient array to at least one second assay, wherein the first assay is different than the second assay. Claims 1 and 88 no longer recite "performing a biological analysis of each substantial copy." Accordingly, the visual inspection analysis that the examiner asserts on page 7 of the Office action is disclosed by Kraaz et al. is not relevant to claims 1 and 88.

For the foregoing reasons alone, the pending §102(b) rejection over Kraaz et al. must be reconsidered and withdraw. However, several of the rejected dependent claims also recite novel features not found in the Kraaz et al. disclosure.

For example, claim 12 contemplates determining whether there are correlations between clinical characteristics associated with each assigned location and the results of the first assay and the second assay. The power of the claimed assays to provide the basis for performing the additional analyses now specifically recited in claims 1 and 88 flows from the present inventors'

novel appreciation that their arrays could provide accurate assay results that could be efficiently correlated with clinical characteristics. The middle column of Kraaz et al. that is cited on page 6 of the Office action as disclosing the subject matter of claim 12 does not, in fact, disclose or suggest performing such correlation. Kraaz et al. simply describes antibody testing of specimens against controls. Such control testing is not a comparison to clinical characteristics.

Claim 14 further emphasizes this distinction by specifically identifying the clinical characteristics as clinical course, treatment response, patient age, tumor grade, tumor size, node status and receptor status. There is no indication in Kraaz et al. that these types of clinical characteristics were even recorded for each specimen, much less correlated with the assay results and then further analyzed as recited in claim 1. Kraaz et al.'s missing disclosure of correlations between assay results and clinical characteristics as recited in claims 12 and 14 is fatal to a rejection under §102(b) for anticipation.

New dependent claim 120 also indicates that at least the first assay or the second assay comprises a nucleic acid analysis, and new dependent claim 121 indicates that at least one of the first agent or the second agent comprises a nucleic acid probe. Kraaz et al. only mentions performing antibody and avidin-biotin complex testing. There is no mention in Kraaz et al. of any type of nucleic acid analysis. Hence, Kraaz et al. does not anticipate or render obvious claims 120 and 121.

Enghardt et al.

Claims 1-20, 29-30, 43-44, 49, 53-61, 70, 87-92, 95-97, 101 and 102 have been rejected under 35 U.S.C. §102(b) over Enghardt et al. Applicants continue to maintain that Enghardt et al. fails to disclose comparing and correlating results from corresponding assigned locations of different substantial copies or different sections. However, in order to advance prosecution, independent claims 1, 16, 53 and 88 have been amended to include a further step specifying additional analysis that is performed based on the correlations or results obtained from the array.

On page 10 of the Office action, the examiner rejected previously pending claim 43 because Enghardt et al. allegedly "disclose the method wherein the analyzing evaluates a reagent for diagnosis i.e. antibody (Fig. 3)." However, the additional analysis step of evaluating "a reagent for disease diagnosis or treatment" that appeared in claim 43 is not included in amended claims 1, 16, 53 and 88. Enghardt et al. does not disclose or suggest that any of the other

specifically claimed additional analyses could be performed using the multitissue control blocks (MTCB) obtained according to Enghardt et al.

In addition, applicants cannot discern any teaching in Enghardt et al. of subjecting successive copies or sections of the array to first and second assays, respectively, that are different to determine if there are correlations between the results of the assays for an assigned specimen location. There is no explicit statement in Enghardt et al. that serial sections (e.g., section #1 and section #2) of the multitissue control block (MTCB) are subjected respectively to different antibody assays (e.g., antibody assay #1 and antibody assay #2) and the results of each assay are compared against each other for a specific specimen or sample (e.g., sample at coordinate [1,1] of section #1 vs. sample at coordinate [1,1] of section #2). On the contrary, the blocks disclosed in Enghardt et al. are referred to as "control" blocks meaning that the results for each antibody test are compared to the patient sample provided on the same slide. (See, Enghardt et al., page 54, column 1, "When placed on the same slide as the patient sample, the multitissue control serves as a convenient record for validation of reactivity"). In other words, there is a comparison internally within each slide between the results for arrayed multitissue control block versus the results for the patient sample. There is no comparison in the Enghardt et al. disclosure between the results of at least first and second assays performed on successive copies or sections of the array, respectively, as recited in claims 1, 16, 53 and 88.

For the foregoing reasons alone, the pending §102(b) rejection over Enghardt et al. must be reconsidered and withdraw. However, several of the rejected dependent claims also recite novel feature not found in the Enghardt et al. disclosure.

For example, claim 12 contemplates determining whether there are correlations between clinical characteristics associated with each assigned location and the results of the first assay and the second assay. The power of the claimed assays to provide the basis for performing the additional analyses now specifically recited in claims 1, 16, 53 and 88 flows from the present inventors' novel appreciation that their arrays could provide accurate assay results that could be efficiently correlated with clinical characteristics. The left column of page 55 of Enghardt et al. that is cited on page 9 of the Office action as supporting a novelty rejection of claim 12 simply indicates that the patient "diagnosis" is recorded for tissue specimens. There is no teaching in Enghardt et. al. that the diagnosis information is correlated with the results of two different assays, and then further analyzed as now recited in claims 1, 16, 53 and 88.

Claim 14 further emphasizes this distinction by specifically identifying the clinical characteristics as clinical course, treatment response, patient age, tumor grade, tumor size, node status and receptor status. There is no indication in Enghardt et al. that these specific types of clinical characteristics were even recorded for each specimen, much less correlated with the assay results and then further analyzed as recited in claim 1. Enghardt et al.'s missing disclosure of correlations between assay results and clinical characteristics as recited in claims 12 and 14 is fatal to a rejection under §102(b) for anticipation.

New dependent claim 120 also indicates that at least the first assay or the second assay comprises a nucleic acid analysis, and new dependent claim 121 indicates that at least one of the first agent or the second agent comprises a nucleic acid probe. Enghardt et al. only describes performing immunohistochemical testing of their tissue block. There is no mention in Enghardt et al. of any type of nucleic acid analysis or the use of a nucleic acid probe. For this reason alone, the pending 35 U.S.C. §102(b) rejection over Enghardt et al. must be withdrawn.

35 U.S.C. §103 rejections

Claims 21, 22, 45-48, 93-94 and 98-100

Claims 21, 22, 45-48, 93-94 and 98-100 have been rejected under 35 U.S.C. §103 over Enghardt et al. Claims 21, 45 and 93-94 have now been canceled. Claims 22, 46-48 and 98-100 all depend from claim 1 which is patentably distinguishable over Enghardt et al. for the reasons expressed above.

Claims 24-29, 31, 50-52, 62-63, 68-69, 71-78 and 86

Claims 24-29, 31, 50-52, 62-63, 68-69, 71-78 and 86 have been rejected under 35 U.S.C. §103 over Enghardt et al. combined with Stapleton et al.

Dependent claim 24 now recites combining the method of claim 1 with "using a nucleic acid microarray to identify a biomarker to be used in the first assay or the second assay, wherein the nucleic acid microarray comprises an arrangement of nucleic acid in assigned locations on a matrix." The nucleic acid microarray recited in claim 24 is not the recipient array, first assay or second assay, of claim 1. The nucleic acid microarray is used separately to identify a biomarker that can then be used in the first or second assay. As pointed out in applicants' August 27, 2004,

response on page 22 Stapleton et al. contains no suggestion to use a nucleic acid array to identify a biomarker that could then be used in a subsequent biological analysis.

The pending Office action at page 19 states that "the instant claims are broadly drawn to microarray, but do not define or limit the microarray structurally so as to define the microarray over the arrayed samples of Example 6 or the arrayed (electrophoresed) fragments illustrated in Fig. 1-6." In example 6 of the Stapleton et al. provisional application RNA amplification of human cells immobilized on a matrix is performed by utilizing a RT-PCR system. Such a RT-PCR system is not "an arrangement of nucleic acid in assigned locations on a matrix." Thus, the array of immobilized cells in Stapleton et al. is not assayed with a nucleic acid microarray.

The pending Office action at page 19 also states that "[a]pplicant asserts that the instantly claimed microarray is defined over the teaching of Stapleton in the instant specification." Applicants' August 27, 2004, response, in fact, argued that the Stapleton et al. provisional application does not disclose a nucleic acid microarray, which has now been more specifically described.

With respect to claims 29 and 50-52, the pending Office action at page 19 contends that Example 6 of the Stapleton et al. provisional application discloses a comparison of arrayed samples. However, as discussed above, Example 6 simply describes RNA amplification of human cells immobilized on a matrix. There is no indication that once the RNA amplification is completed and analyzed that the result of each RNA analysis is then compared to another result of a different biological analysis for each of the immobilized human cell samples. Thus, Example 6 does not, in fact, teach parallel analysis.

With respect to claims 62, 63, 68, 69, 71-78 and 86, applicants reiterate the arguments set forth in their August 27, 2004, reply since it does not appear that the pending Office action addressed these specific arguments.

Claims 32-42

Claims 32-42 have been rejected under 35 U.S.C. §103 over Stapleton et al. combined with An et al. Claim 32 has been amended to describe the nucleic acid array with more specificity. There is no mention in An et al. of such nucleic acid arrays meaning that the combination of Stapleton et al. and An et al. would not have suggested any methodology that utilizes nucleic acid arrays. An et al. is also fatally silent with regard to the use of nucleic acid

probes to select a nucleic acid array. In summary, there is nothing in either Stapleton et al. or An et al. combined that would have suggested the analysis strategy first envisioned by the applicants as set forth in claim 32.

Claims 66 and 67

Claims 66 and 67 have been rejected under 35 U.S.C. §103 over Enghardt et al. combined with Stapleton et al. and An et al. Claims 66 and 67 depend from claim 53. As discussed above in connection with the 35 U.S.C. §102 rejection of claim 53, Enghardt et al. fails to describe or suggest exposing at least one successive sequential copies of the matrix to different agents. Stapleton et al. and An et al. also do not disclose or suggest such sequential exposure. For this reason alone, the asserted combination of Enghardt et al., Stapleton et al. and An et al. does not establish a case of *prima facie* obviousness with respect to claims 66 and 67.

It is respectfully submitted that the present claims are in condition for allowance. Should there be any questions regarding this application, Examiner Forman invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 
Wayne W. Rupert
Registration No. 34,420

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 228-9446